UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/519,193	12/21/2005	Heinrich Haas	062587-5003	6810

9629 7590 05/12/2009
MORGAN LEWIS & BOCKIUS LLP
1111 PENNSYLVANIA AVENUE NW
WASHINGTON, DC 20004

EXAMINER	
SHOMER, ISAAC	
ART UNIT	PAPER NUMBER
1612	
MAIL DATE	DELIVERY MODE
05/12/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/519,193	HAAS ET AL.	
	Examiner	Art Unit	
	ISAAC SHOMER	4121	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-59* is/are pending in the application.

4a) Of the above claim(s) *28,33,36-53 and 55-59* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-27,29-32,34-35, and 54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11 April 2006, 14 August 2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application is a national stage application of PCT/EP03/06760, filed 26 June 2003. Claims 24-27, 29-32, 34-35, and 54 are included in the prosecution.

Priority

Priority is claimed under 35 U.S.C. 119(e) to provisional applications 60/391,244, filed 26 June 2006 and 60/391,246, filed 26 June 2006. Priority is claimed under 35 U.S.C. 119(a)-(d) to application EP 020189072, filed 23 August 2002. A certified copy of the foreign priority application has been filed.

Election/Restriction

Applicant's election with traverse of Group I, claims 24-35 and 54 in the reply filed on 17 April 2009 is acknowledged. The traversal is on the ground(s) that the combination of Yang and Ray do not render the claimed invention obvious. In light of this, the lack of unity requirement between Yang and Ray is withdrawn, and there is a new lack of unity requirement in light of Wall et al. (US Patent 4,981,968).

The inventions listed as Groups I-IV do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The special technical feature of Group I is a composition comprising camptothecin in the carboxylate form associated with an organic cationic molecule. The composition of claim 24 does not present a contribution over the prior art. As disclosed

in Wall et al. (US Patent 4,981,968) (Column 4, Lines 33-52), the composition comprising carboxylate camptothecin with an organic cation of instant claim 24 is not novel. As such, Group I does not share a special technical feature with the instant claims of Group II-IV. Therefore, the claims are not so linked within the meaning of PCT Rule 13.2 so as to form a single inventive concept, and unity between Groups I-IV is broken.

Furthermore, applicant argues that there is no search burden in regards to searching all of the groups.

This is not found persuasive because the requirement of search burden applies only to U.S. restrictions filed under 35 U.S.C. 121. As the instant application is a national stage application, the requirement of search burden does not apply.

The requirement is still deemed proper and is therefore made FINAL.

Claims 36-59 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected group, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 17 April 2009.

Applicant's election with traverse of the following species:

A lipid, as of claim 26

A quaternary ammonium group, as of claims 27 and 29.

A polyelectrolyte, as of claim 30.

A lipid for anionic/neutral amphiphile, as of claim 32

A phospholipid as of claim 34

in the reply filed on 17 April 2009 is acknowledged. The traversal is on the ground(s) that there is no lack of unity for the reasons shown supra, and that there is no search burden. This is not found persuasive because of the reasons shown supra.

The requirement is still deemed proper and is therefore made FINAL.

Claims 28 and 33 withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected specie (tertiary amino group of claim 28 and sterol of claim 33), there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 17 April 2009.

Claim Rejections - 35 USC § 112 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 24-27, 29-32, 34-35 and 54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. The term "substantially free" in claim 24 is a relative term which renders the claim indefinite. The term "substantially free" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The term

"virtually free" is defined by the specification, whereas the term "substantially free" is not defined by the specification.

2. Claim 24 recites the limitation "at least about." The term "at least" delineates only numerical values more than the recited value where the term "about" may be less than or more than the recited value. Because of the conflict of terms, it is unclear which term is limiting. See also MPEP 2173.05(b) (citing Amgen v. Chugai, 18 USPQ2d 1016 (Fed. Cir. 1991), in which the phrase "at least about" was held indefinite).

Where values can vary depending on the basis for their determination, the claimed subject matter may be indefinite. *See* Honeywell Intl. v. Intl. Trade Commn., 341 F.3d 1332, 1340 (Fed. Cir. 2003). (Holding that, where a claimed value varies with its method of measurement and several alternative methods of measurement are available, the value is indefinite when the claim fails to concurrently recite the method of measurement used to obtain it). Accordingly, the ratios recited by instant claims, which is 1:1 of organic cationic molecule to carboxylate, are incomplete insofar as they do not specify the frame of reference used to measure them, e.g., HPLC, ion chromatograph etc.

In order to overcome this ground of rejection the examiner recommends specifically defining the claimed range.

3. Claim 54 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "pharmaceutically effective amount" in claim 54 is indefinite since the disease to be treated is not recited.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 24 and 54 are rejected under 35 U.S.C. 102(b) as being anticipated by Wall et al. (US Patent 4,981,968).

Wall et al. (US Patent 4,981,968), (hereafter referred to as Wall), column 4 lines 33-52 teaches water soluble camptothecin analogs with a free carboxyl group comprising an organic cation, (e.g. ammonium salts). As the carboxyl group is free, said composition is substantially free of lactone form. As cations reaction with anions in a molar ratio; that is, one cation reacts with one anion, the prior art meets the instant requirement of "at least about 1:1."

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1. Claims 25-27, 29, 31-32 and 34-35 and 54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wall et al. (US Patent 4,981,968) in view of Eppstein et al. (US Patent 4,897,355).

Wall, column 4 lines 33-52, teaches the composition comprising camptothecin in its carboxylate form with an organic cationic molecule. See supra rejection of claim 24.

Wall does not teach an embodiment wherein said camptothecin carboxylate is associated with a cationic amphiphile (e.g. DOTMA).

Eppstein et al. (US Patent 4,897,355) (hereafter referred to as Eppstein) teaches, in column 16 lines 13-27, a liposome comprising DOTMA vesicles (instant claims 25-27 and 29; DOTMA is the amphiphile of instant claim 29). Said liposome also optionally

comprises DOPC (reading on diacylphosphatidylcholine, instant claims 31-32 and 34-35). The combination of DOTMA and DOPC is a pharmaceutically acceptable carrier.

It would have been prima facie obvious at the time the invention was made to have used the liposome comprising DOTMA, of Eppstein, to deliver the camptothecin-carboxylate of Wall. Eppstein, column 4 lines 49-54 teaches the positively charged liposomes, (which may be obtained by incorporating cationic liposomes such as DOTMA) target the negatively charged cell surface. This brings pharmaceutical materials (e.g. camptothecin-carboxylate) directly to the cell surface. This results in better uptake of the active agent, which results in a greater effective dose as well as lower side effects (as the drug goes only where it is supposed to go). Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to encapsulate camptothecin-carboxylate, of Wall, into a DOTMA containing liposome, with a reasonable expectation of success in improved uptake of camptothecin-carboxylate.

2. Claims 24-25 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wall et al. (US Patent 4,981,968) in view of Prakash et al. (US Patent 5,654,484).

Wall, column 4 lines 33-52, teaches the composition comprising camptothecin in its carboxylate form with an organic cationic molecule. See supra rejection of claim 24.

Wall does not teach an embodiment wherein said camptothecin carboxylate is associated with a cationic polymer that is a polyelectrolyte.

Prakash et al. (US Patent 5,654,484) (hereafter referred to as Prakash) teaches in the abstract, a cationic polyamine. Polyamines have an antineoplastic effect, according to Prakash, Title. Said antineoplastic comounds are therapeutically effective in patients with diseases involving rapidly progressing cell growth associated with the neoplasm (e.g. cancer), as in Prakash, column 1 lines 20-35.

It would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to have combined the polyamine with the camptothecin carboxylate of Wall et al. Prakash, abstract, shows that polyamines (which are cationic polyelectrolytes) have antineoplastic effects. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to combine an antineoplastic drug with an antineoplastic polyelectrolyte with an expectation of obtaining at least an additive effect. Since the polyamines taught by Prakash are cationic, one would expect them to react with the carboxylic group in the camptothecin of Wall.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ISAAC SHOMER whose telephone number is (571)270-7671. The examiner can normally be reached on Monday - Thursday 7:30AM - 5:00 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Fred Krass can be reached on (571)272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/I. S./
Examiner, Art Unit 1612
/Gollamudi S Kishore /
Primary Examiner, Art Unit 1612